Cigarette Smoking, Metabolic Gene Polymorphism, and Psoriasis

Journal of Investigative Dermatology (2006) **126,** 693–694. doi:10.1038/sj.jid.5700161; published online 12 January 2006

TO THE EDITOR

Environmental and genetic factors have been found to influence manifestation and severity of psoriasis. The most prominent environmental factor possibly leading to psoriasis is smoking and the related nicotine exposure, as was again discussed in this year's publication with data from an Italian case–control study (Naldi *et al.*, 2005). Among the genetic factors that have been found to influence psoriasis are also key detoxifying enzymes metabolizing toxins from tobacco smoke. Variant alleles of *CYP1A1*, which code for enzymes with higher activity, were found to protect against psoriasis in a study carried out by our group (Richter-Hintz *et al.*, 2003).

If smoking and the related nicotine exposure is a risk factor for psoriasis, then the association between psoriasis and the non-variant genotype of *CYP1A1*, which codes for enzymes with lower activity should be stronger in smokers than in non-smokers. This was investigated with the data from our study (Richter-Hintz *et al.*, 2003) where the influence of smoking was not evaluated so far. Interactions between smoking and *CYP1A1* polymorphisms have been found for a number of other diseases including arteriosclerosis (Wang *et al.*, 2002a) and adverse birth outcomes (Wang *et al.*, 2002b), but have not been investigated for psoriasis before.

Our study on genetic factors of psoriasis was approved by the local ethical committee. The 321 Caucasian psoriasis patients and 235 unrelated controls gave written consent before being recruited. Standardized interviews were performed, and begin, end, amount, and frequency of smoking and alcohol consumption were asked for. Subjects were assigned smoker, ex-smoker, and non-smoker accordingly.

CYP1A1 polymorphisms (alleles *1A, *2A, and *2C) were determined by restriction fragment length polymorphism as described (Richter-Hintz *et al.*, 2003). Allele *1A is the non-variant sequence, *2A has a 3801 T>G exchange, and *2C has a 2455A>G exchange.

Logistic regression was used for analysis. The *CYP1A1* genotype with no variant alleles was coded as 1 and the others as zero. Gender and age were included as covariates. The analysis was done for never-smokers, ex-smokers and smokers separately.

Of the controls 56% were never smokers, 24% were ex-smokers, and 20% were smokers, and in the psoriasis cases, 32% never smoked, 25% gave up smoking, and 43% were smokers. This difference in smoking behavior was highly significant (χ^2-test, $P<0.0001$). Thirteen percent of the controls and 12% of the cases stated that they drank alcohol every day (no significant difference).

Table 1 demonstrates that the non-variant genotype of *CYP1A1*, which codes for enzymes with lower activity was significantly associated with psoriasis in smokers, less in ex-smokers but not in non-smokers. In controls, the frequency of the non-variant genotype does not vary across the strata defined by smoking behavior, whereas in psoriasis cases, this genotype was more often in smokers than in never smokers.

The associations found strengthen the view that smoking might cause the manifestation of psoriasis. A modification of the effect of smoking by *CYP1A1* polymorphisms was already investigated in cancer, arteriosclerosis, and adverse birth outcomes. In all these cases, however, the smoking-related risks were more frequent in the variant genotypes, where enzyme activity is increased. This is different in psoriasis. The mechanism by which smoking affects psoriasis might be different from the mechanism in cancer, arteriosclerosis, and adverse birth outcomes. The risk association identified here indirectly points to non-metabolized xenobiotics as etiological agents of psoriasis. Nicotine might be a candidate.

Table 1. Frequency of the non-variant *CYP1A1* genotype in psoriasis cases and controls stratified by smoking behavior

	Psoriasis cases[1] (%) (*n*)	Controls[1] (%) (*n*)	Adjusted[2] odds ratio (95% confidence interval)	*P*-value
Never smokers	81.8 (88)	75.0 (116)	1.64 (0.80–3.38)	0.1766
Ex-smokers	88.2 (68)	76.5 (51)	2.88 (1.03–8.03)	0.0431
Smokers	91.7 (120)	76.2 (42)	3.56 (1.35–9.37)	0.0103
All	87.7 (276)	75.6 (209)	2.48 (1.52–4.03)	0.0003

[1]Only cases and controls with complete information about smoking behavior were included in the calculation.
[2]Adjusted for age and gender.

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